

eTable 1. Childhood treatment of the 59 ADHD male probands with anatomic MRI data at adult follow-up at mean age 41 (41FU)

Medication	Number of Subjects Treated with Medication N(%)	Cumulative Number of Days Treated with Indicated Medication [not necessarily consecutive days]				
		Mean	Median	SD	Mini-Mum	Maxi-mum
Methylphenidate	55 (93)	789.9	613	640.2	9	2486
Dextroamphetamine	10 (17)	300.7	176	353.6	22	1202
Pemoline	3 (5)	205.0	222	44.0	155	238
Any of Above*	55 (93)	855.7	735	660.1	9	2486
Imipramine	10 (17)	186.4	109.5	182.4	71	664
Thioridazine	34 (58)	242.1	149	203.5	3	682

*All the individuals who were treated with dextroamphetamine or pemoline were also treated with methylphenidate

eTable 2. Grey matter density and cortical thickness within clusters for subgroups of controls with ADHD-NOS and probands with ADHD-NOS at 41FU

Regions	Controls with ADHD-NOS (n=23)		Probands with ADHD-NOS (n=16)	
	mean	SD	mean	SD
Grey matter density clusters				
L Sup Parietal (BA7)	0.42	0.04	0.41	0.05
L Cerebellum	0.55	0.15	0.51	0.08
L Inf Cerebellum	0.41	0.17	0.34	0.13
L Middle Temporal gyrus (BA21)	0.37	0.09	0.38	0.08
L Temporo-occipital (BA37)	0.57	0.09	0.57	0.08
Brainstem extending to Cerebellum	0.32	0.14	0.27	0.08
L Temporal-parahippocampal (BA35)	0.74	0.07	0.72	0.06
L Frontal pole (BA10)	0.45	0.06	0.43	0.07
R Parietal Postcentral (BA3) extending to BA6	0.40	0.05	0.40	0.05
R Cerebellum	0.49	0.19	0.46	0.1
R Thalamus	0.72	0.11	0.71	0.1
R Occipital, Cuneus (BA18/19)	0.65	0.07	0.65	0.06
R Sup Frontal gyrus (BA10)	0.47	0.06	0.45	0.05
R Frontal lobe (BA6)	0.47	0.09	0.44	0.09
R Middle Frontal gyrus (BA10) extending to Orbitofrontal cortex (BA11)	0.49	0.07	0.47	0.06
R Temporal Fusiform (BA36)	0.64	0.07	0.64	0.07
R Caudate	0.52	0.11	0.48	0.11
R Middle Temporal (BA21) extending to (BA38)	0.55	0.07	0.54	0.08
R Middle Temporal (BA21) extending to (BA38)	0.51	0.07	0.49	0.08
Anterior Cingulate/limbic(BA24)	0.80	0.05	0.78	0.04
Cortical thickness clusters (mm)				
L Sup Parietal (BA7)	2.95	0.18	2.85	0.17
L Precentral G (BA6)	3.34	0.16	3.26	0.15
L Sup Temp G (BA38)	3.73	0.23	3.60	0.23
L Frontal Pole (BA10)	3.19	0.22	3.06	0.18
L Cuneus (BA19)	2.79	0.15	2.65	0.17
L Precuneus (BA31)	3.28	0.20	3.23	0.19
R Precuneus (BA7)	3.18	0.20	3.12	0.13
R Inf Parietal (BA40)	3.01	0.17	2.91	0.18
R Sup Temp G (BA38)	3.87	0.29	3.62	0.25
R Temporal G extending to Insula (BA13)	3.79	0.22	3.69	0.24
R Precentral G (BA6)	3.38	0.21	3.27	0.19
R Frontal Pole (BA10)	3.38	0.15	3.28	0.17
R Middle Frontal G (BA9)	3.41	0.25	3.19	0.18
R Occipital (BA19)	2.98	0.19	2.86	0.19
R Occipital (BA18)	2.75	0.15	2.69	0.21

BA: Brodmann area; L: Left; R: Right; Sup: Superior; Inf: Inferior

eTable3
Participants with vs. without Anatomic MRIs

STAGE 1 CONTRASTS-
ALL SUBJECTS WITH DATA AT Late Adolescent ASSESSMENT AT Mean Age 18 [18FU]

Classification of All Male Subjects		
Assessments	Probands (n = 207) N	Controls (n = 178) N
MRI Completed, 18FU Diagnostic Data Obtained	59	81
MRI Not Completed, 18FU Diagnostic Data Obtained	136	97
SUBTOTAL	195	178**
MRI Completed, No 18FU Data Obtained	2	0
MRI Not Completed, No 18FU Data Obtained	10*	0

*7 of these Probands did not have any follow-up data (18FU, 25FU, or 41FU)

**All 178 Controls were recruited at 18FU

The following Stage 1 Contrasts were based on the 195 Male Probands and 178 Male Controls with 18FU data. Analyses in eTable3 include 2 Probands and 1 Control who were scanned at 41FU but whose data did not pass quality control criteria.

eTable3a
Ongoing (at 18FU) Diagnostic Status of Probands

Ongoing (at 18FU) DSM-III Late Adolescent Diagnoses	Definite Only			Probable or Definite		
	Probands w/MRIs (n=59) N (%)	Probands w/o MRIs (n=136) N (%)	p (2- tailed)	Probands w/MRIs (n=59) N (%)	Probands w/o MRIs (n=136) N (%)	p (2- tailed)
Antisocial Personality/ Conduct Disorder	15 (25)	36 (27)	.88	20 (34)	39 (29)	.47
Alcohol SUD*	7 (12)	3 (2)	.005	8 (14)	6 (4)	.02
Non-Alcohol SUD**	11 (19)	10 (7)	.02	13 (22)	12 (9)	.01
Any SUD**	15 (25)	11 (8)	.001	16 (27)	16 (12)	.01
Any Mood Disorder	0	0	---	1 (2)	2 (2)	.91
Any Anxiety Disorder	0	1 (1)	.51	0	1 (1)	.51
Any DSM-III Dis.***	22 (37)	40 (29)	.28	26 (44)	45 (33)	.14

*SUD = Substance Use Disorder

**Excluding Nicotine Dependence

***Excluding Attention Deficit Disorder (rates shown in eTable3c and eTable3d)

eTable3b
Ongoing (at 18FU) Diagnostic Status of Controls

Ongoing (at 18FU) DSM-III Late Adolescent Diagnoses	Definite Only			Probable or Definite		
	Controls w/MRIs (n=81) N (%)	Controls w/o MRIs (n=97) N (%)	p (2- tailed)	Controls w/MRIs (n=81) N (%)	Controls w/o MRIs (n=97) N (%)	p (2- tailed)
Antisocial Personality/ Conduct Disorder	5 (6)	7 (7)	.78	6 (7)	8 (8)	.84
Alcohol SUD*	3 (4)	5 (5)	.64	5 (6)	7 (7)	.78
Non-Alcohol SUD**	2 (3)	1 (1)	.46	3 (4)	1 (1)	.23
Any SUD**	4 (5)	6 (6)	.72	6 (7)	8 (8)	.84
Any Mood Disorder	0	2 (2)	.19	1 (1)	3 (3)	.41
Any Anxiety Disorder	3 (4)	0	.06	3 (4)	0	.06
Any DSM-III Dis.***	10 (12)	12 (12)	.99	16 (20)	15 (16)	.45

*SUD = Substance Use Disorder

**Excluding Nicotine Dependence

***Excluding Attention Deficit Disorder (rates shown in eTable3c and eTable3d)

eTable3c
Ongoing (at 18FU) Attention Deficit Disorder in Probands

Ongoing (at 18FU) DSM-III Late Adolescent ADD Symptoms and Diagnosis	Probands with MRIs (n=59) N (%)	Probands without MRIs (n=136) N (%)	p (2-tailed)
Definite Attention Deficit Disorder with/without Hyperactivity	21 (36)	50 (37)	.88
Clinically Significant			
Inattention	30 (51)	64 (47)	.63
Impulsivity	30 (51)	67 (49)	.84
Hyperactivity	24 (41)	47 (35)	.42

eTable3d
Ongoing (at 18FU) Attention Deficit Disorder in Controls

Ongoing (at 18FU) DSM-III Late Adolescent ADD Symptoms and Diagnosis	Controls with MRIs (n=81) N (%)	Controls without MRIs (n=97) N (%)	p (2-tailed)
Definite Attention Deficit Disorder with/without Hyperactivity	3 (4)	2 (2)	.51
Clinically Significant			
Inattention	7 (9)	10 (10)	.71
Impulsivity	7 (9)	11 (11)	.55
Hyperactivity	7 (9)	5 (5)	.36

eTable3e
Childhood Characteristics of Probands

Variable	Probands with MRIs (n=59)	Probands without MRIs (n=136)	p (2-tailed)
	Mean (SD)	Mean (SD)	
Age at Referral (months)	99.4 (20.4)	100.8 (19.4)	.63
SES at Referral*	3.3 (0.9)	3.2 (1.1)	.49
WISC Full Scale IQ	105.6 (12.4)	103.5 (11.8)	.26
Conners Hyperactivity Factor**	2.2 (0.5)	2.1 (0.4)	.39

*Hollingshead & Redlich, (1958) based on parent education and occupation (1-Upper class to 5-Lower class)

**Based on the Conners Teacher Rating Scale (0-Not at all to 3-Very much)

**STAGE 2 CONTRASTS-
SUBJECTS KNOWN TO BE DECEASED
AT 41FU REMOVED**

At follow-up at mean age 41 (41FU), 15 Probands and 5 Controls were known to be deceased. However, 1 of these Probands had not participated in any of the follow-ups (18FU, 25FU, or 41FU). Therefore, the following Stage 2 Contrasts were based on 181 Male Probands (i.e., 195 minus 14) and 173 Male Controls (i.e., 178 minus 5) who were not known to be deceased at 41FU, and who had 18FU data. Analyses include 2 Probands and 1 Control who were scanned at 41FU but whose data did not pass quality control criteria.

eTable3f Ongoing (at 18FU) Diagnostic Status of Probands Not Known to be Deceased at 41FU						
Ongoing (at 18FU) DSM-III Late Adolescent Diagnoses	Definite Only			Probable or Definite		
	Probands w/MRIs (n=59) N (%)	Probands w/o MRIs (n=122) N (%)	p (2- tailed)	Probands w/MRIs (n=59) N (%)	Probands w/o MRIs (n=122) N (%)	p (2- tailed)
Antisocial Personality/ Conduct Disorder	15 (25)	32 (26)	.91	20 (34)	35 (29)	.48
Alcohol SUD*	7 (12)	2 (2)	.003	8 (14)	5 (4)	.02
Non-Alcohol SUD**	11 (19)	9 (7)	.02	13 (22)	11 (9)	.02
Any SUD**	15 (25)	10 (8)	.002	16 (27)	15 (12)	.01
Any Mood Disorder	0	0	---	1 (2)	2 (2)	.98
Any Anxiety Disorder	0	1 (1)	.49	0	1 (1)	.49
Any DSM-III Dis.***	22 (37)	36 (30)	.29	26 (44)	40 (33)	.14

*SUD = Substance Use Disorder

**Excluding Nicotine Dependence

***Excluding Attention Deficit Disorder (rates shown in eTable3h and eTable3i)

eTable3g
Ongoing (at 18FU) Diagnostic Status of Controls
Not Known to be Deceased at 41FU

Ongoing (at 18FU) DSM-III Late Adolescent Diagnoses	Definite Only			Probable or Definite		
	Controls w/MRIs (n=81) N (%)	Controls w/o MRIs (n=92) N (%)	p (2- tailed)	Controls w/MRIs (n=81) N (%)	Controls w/o MRIs (n=92) N (%)	p (2- tailed)
Antisocial Personality/ Conduct Disorder	5 (6)	5 (5)	.84	6 (7)	6 (7)	.82
Alcohol SUD*	3 (4)	4 (4)	.83	5 (6)	5 (5)	.84
Non-Alcohol SUD**	2 (3)	1 (1)	.49	3 (4)	1 (1)	.25
Any SUD**	4 (5)	5 (5)	.88	6 (7)	6 (7)	.82
Any Mood Disorder	0	1 (1)	.35	1 (1)	2 (2)	.64
Any Anxiety Disorder	3 (4)	0	.06	3 (4)	0	.06
Any DSM-III Dis.***	10 (12)	9 (10)	.59	16 (20)	12 (13)	.23

*SUD = Substance Use Disorder

**Excluding Nicotine Dependence

***Excluding Attention Deficit Disorder (rates shown in eTable3h and eTable3i)

eTable3h
Ongoing (at 18FU) Attention Deficit Disorder in Probands
Not Known to be Deceased at 41FU

Ongoing (at 18FU) DSM-III Late Adolescent ADD Symptoms and Diagnosis	Probands with MRIs (n=59) N (%)	Probands without MRIs (n=122) N (%)	p (2-tailed)
Definite Attention Deficit Disorder with/without Hyperactivity	21 (36)	43 (35)	.96
Clinically Significant			
Inattention	30 (51)	57 (47)	.60
Impulsivity	30 (51)	60 (49)	.83
Hyperactivity	24 (41)	41 (34)	.35

eTable3i
Ongoing (at 18FU) Attention Deficit Disorder in Controls
Not Known to be Deceased at 41FU

Ongoing (at 18FU) DSM-III Late Adolescent ADD Symptoms and Diagnosis	Controls with MRIs (n=81) N (%)	Controls without MRIs (n=92) N (%)	p (2-tailed)
Definite Attention Deficit Disorder with/without Hyperactivity	3 (4)	2 (2)	.55
Clinically Significant			
Inattention	7 (9)	9 (10)	.80
Impulsivity	7 (9)	10 (11)	.62
Hyperactivity	7 (9)	5 (5)	.41

eTable3j
Childhood (Time 1) Characteristics of Probands
Not Known to be Deceased at 41FU

Variable	Probands with MRIs (n=59)	Probands without MRIs (n=122)	p (2-tailed)
	Mean (SD)	Mean (SD)	
Age at Referral (months)	99.4 (20.4)	101.1 (19.7)	.58
SES at Referral*	3.3 (0.9)	3.2 (1.1)	.41
WISC Full Scale IQ	105.6 (12.4)	103.0 (11.6)	.17
Conners Hyperactivity Factor**	2.2 (0.5)	2.1 (0.4)	.41

*Hollingshead & Redlich, (1958) based on parent education and occupation (1-Upper class to 5-Lower class)

**Based on the Conners Teacher Rating Scale (0-Not at all to 3-Very much)

eTable 4. Demographic characteristics of the 139 ADHD probands and non-ADHD male controls with analyzable anatomic MRI data at 41FU

Adult Variable	Probands without ADHD (remitters) (n = 26)	Probands with Persistent ADHD (n = 17)	Probands with ADHD NOS (n = 16)	Non-ADHD Controls (n = 57)	Controls with ADHD NOS (n = 23)	F	p (two-tailed)
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)		
Age at Follow-Up (Years)	41.0 (2.5)	41.2 (2.7)	41.0 (3.0)	41.3 (3.0)	41.5 (3.5)	0.12	0.98
Socioeconomic Status* at 41FU	3.2 (1.1) ^A	3.7 (1.2) ^{B,C}	3.4 (1.0) ^D	2.4 (1.1) ^{A,B,D}	2.7 (.9) ^C	7.1	0
Educational Attainment**	13.9 (2.8) ^E	13.7 (2.1) ^F	12.7 (2.1) ^{G,H}	15.7 (2.2) ^{E,F,G}	15.4 (2.4) ^H	7.78	0
WASI*** Full Scale IQ	104.2 (11.8)	100.7 (13.4)	97.1 (14.7) ^I	111.9 (12.7) ^I	104.8 (18.6)	4.56	0.002
Global Assessment Scale Rating****	67.5 (14.9)	61.5 (8.9) ^J	58.8 (9.7) ^K	73.5 (10.5) ^{J,K,L}	65.9 (8.3) ^L	8.23	0

Hollingshead and Redlich (1958) scale, based on the participant's education and occupation. This 5-point scale ranges from 1-upper social class to 5-lower social class.

**Highest Grade Completed (12- high school, 16- 4 years of college, etc.)

***Wechsler Abbreviated Scale of Intelligence. WASIs were only obtained on 74 (92%) of the 80 Controls.

****The Global Assessment Scale was completed by the "blind" clinician that conducted the diagnostic assessment.

Pairwise comparisons using Tukey's HSD

^A pairwise comparison significant ($p = .024$)

^B pairwise comparison significant ($p < .001$)

^C pairwise comparison significant ($p = .028$)

^D pairwise comparison significant ($p = .006$)

^E pairwise comparison significant ($p = .008$)

^F pairwise comparison significant ($p = .014$)

^G pairwise comparison significant ($p < .001$)

^H pairwise comparison significant ($p = .006$)

^I pairwise comparison significant ($p = .003$)

^J pairwise comparison significant ($p = .001$)

^K pairwise comparison significant ($p < .001$)

^L pairwise comparison significant ($p = .042$)

eTable 5. Comorbidity of adult mental disorders among the 59 ADHD male probands and the 80 non-ADHD male comparisons with analyzable anatomic MRI data at 41FU

Ongoing DSM-IV Disorder (Past 6 Months)	Probands (n = 59) N (%)	Comparisons (n = 80) N (%)	χ^2	p (2 tailed)
Attention Deficit Hyperactivity Disorder				
Full DSM-IV-TR Criteria*	17 (29)	0	26.26	.001
Not Otherwise Specified (NOS)	16 (27)	23 (29)	0.04	.83
Either of Above	33 (56)	23 (29)	10.43	.001
Antisocial Personality Disorder	9 (15)	0	13.05	.001
Substance Use Disorder				
Alcohol	2 (3)	14 (18)	6.64	.01
Non-Alcohol**	9 (15)	6 (8)	2.12	.15
Either of Above**	11 (19)	16 (20)	.04	.84
Mood Disorder	5 (8)	7 (9)	0.00	--
Anxiety Disorder	8 (14)	4 (5)	3.15	.12
ANY DSM-IV DISORDER***	26 (44)	27 (34)	1.53	.22
*Inattentive, Hyperactive-Impulsive, or Combined				
**excluding Nicotine Dependence				
***excluding ADHD and Nicotine Dependence				

eTable 6. Significant (FDR 0.05) cortical thickness clusters without or with adjustment for IQ in inclusive analyses. See Figure 1 and eFigure1.

Without IQ as covariate			With IQ as covariate		
Region	MNI coordinates	vertices #	Region	MNI coordinates	vertices #
L Sup Parietal (BA7)	-26, -55, 68	4,290	L Sup Parietal (BA7)	-25, -55, 68	827
L Precentral G (BA6)	-35, 37, 36	784	L Precentral G (BA6)	-45, -13, 53	115
L Sup Temp G (BA38)	-54, 10, -22	915	L Sup Temp G (BA38)	-54, 10, 22	108
L Frontal Pole (BA10)	-31, 62, -6	638	L Frontal Pole (BA10)	-31, 62, -6	179
L Cuneus (BA19)	-13, -91, 35	618			
L Precuneus (BA31)	-6, -65, 30	62			
R Precuneus (BA7)	10, -73, 51	1148			
			R Inf Parietal (BA40) extending to BA6	49, -40, 50	2,693
R Inf Parietal (BA40)	49, -40, 50	4836	R Sup Temp G (BA38)	30, 15, -40	374
R Sup Temp G (BA38)	30, 15, -40	1141			
R Temporal G extending to Insula (BA13)	48, -1, -3	315			
R Precentral G (BA6)	58, 0, 36	315			
R Frontal Pole (BA10)	27, 47, 32	98			
R Middle Frontal G (BA9)	25, 47, -14	130			
R Occipital (BA19)	27, -87, 26	210			
R Occipital (BA18)	10, -80, 10	94			

L: Left; BA: Brodmann area; G: Gyrus; Sup: Superior; R: Right; Inf: Inferior